Effects of a Low Carbohydrate Diet on Type 2 Diabetics – A Systematic Review of the Literature

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Purpose of this review: To determine whether type 2 diabetics treated with a low carbohydrate diet of at least four weeks duration have better intermediate outcomes, including glycemic control, hemoglobin A1c (HbgA1c), weight reduction, insulin sensitivity, triglycerides (TG), and lipid levels compared to type 2 diabetics on a heart healthy or normal diet?

Background/Introduction

type 2 Diabetes

Type 2 diabetes is a chronic disease that affects a growing number of Americans. Nearly 18.2 million Americans suffer from the disease today.[15] As the average age of the United States population has increased, so has the incidence of obesity, hypertension, glucose intolerance, dyslipidemia, and type 2 diabetes. In fact, the prevalence of type 2 diabetes has slowly risen over the past three decades, roughly paralleling the increase in the proportion of people, including children and young people, who are either overweight or obese.[5] The prevalence of type 2 diabetes in adults ages 40-74 increased from 8.9% during 1976-80 to 12.3% during 1988-1994.[4] Furthermore, type 2 diabetes is being diagnosed more frequently among younger and younger cohorts.

Type 2 diabetes is a leading cause of morbidity and mortality in the United States, and is associated with both microvascular and macrovascular complications.[7] Debilitating microvascular complications include blindness and kidney failure.[8]

Macrovascular complications, which comprise the majority of the morbidity and mortality associated with diabetes,[17] include heart disease, stroke,

and amputation.[17] Diabetics have a 2- to 4-fold higher risk of both coronary artery disease and stroke than non-diabetics. In 2003, the number of deaths directly attributable to diabetes was 47.7 per 10,000 individuals.[15]

In addition, diabetes is a disease of economic significance to the U.S. health care system. The U.S. spent over 98 billion dollars on medical care and lost productivity for type 2 diabetics in the 1997 fiscal year.[18]

Current evidence suggests that tight glycemic control is the best way to prevent many of the microvascular complications of type 2 diabetes. Several studies have provided substantial evidence to support tight glycemic control. For example, the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) both showed that tight glycemic control plays an important role in preventing the microvascular complications of diabetes, including retinopathy, neuropathy, and nephropathy.[19,20]

The UKPDS enrolled 3,867 newly diagnosed type 2 diabetics. The patients were randomized either to conventional diet control, sulphonylurea, or insulin therapy. Over ten years, hemoglobin A_{1C} was 7.0% in the intensive therapy groups (i.e. sulphonylurea, insulin) compared to 7.9% in the conventional diet group. The result was a highly significant 25% reduction in the number of microvascular endpoints. There was no significant difference between insulin therapy and treatment with a sulphonylurea. None of the individual drugs had an adverse effect on cardiovascular outcomes, but all intensive treatment increased the risk of hypoglycemia. Although the UKPDS data suggested a trend toward

reduction in macrovascular outcomes, including amputation and myocardial infarction, convincing data in this area are lacking.[20].

Thus, intensive blood-glucose control in patients with type 2 diabetes substantially decreases the risk of microvascular complications but not macrovascular disease. Tight glycemic control may best be achieved through a combination of pharmacotherapy and lifestyle modifications.[21]

Diet Therapy for Diabetes

Dietary changes are one important lifestyle modification that play an important role in managing diabetes. In both the UKPDS and DCCT, dietary interventions played a key role in glycemic control.[21,22] Several additional studies have documented the effectiveness of dietary interventions in type 2 diabetics. One study showed a 2.0% absolute decrease in HbA_{1c} in patients with newly diagnosed type 2 diabetes.[23] Another study demonstrated a 1.0% absolute decrease in HbA_{1c} in patients with an average 4-year duration of type 2 diabetes.[24]

In addition to tight glycemic control, other risk factors for cardiovascular disease, such as hyperlipidemia and hypertension, are treated concurrently to further lower risk. In fact, the UKPDS studies failed to demonstrate that tight glycemic control leads to a decrease in macrovascular outcomes; the possibility exists that other risk factors (e.g. hyperlipidemia, hypertension) for cardiovascular disease may be more important. Thus, it is imperative that dietary recommendations for diabetics address other risk factors for cardiovascular disease in addition to glycemia.

Rationale for this study

In the middle of a rapidly growing obesity epidemic, patients are constantly bombarded with fad diets and promises of amazing weight loss and health benefits. Low-carbohydrate diets have recently resurfaced as a means of rapid weight loss. Especially popular is the low carbohydrate diet promoted by Robert Atkins, MD, requiring individuals to consume <20grams (g) of carbohydrate a day during the initial stage of the diet. Because, by definition, these diets are low in carbohydrates, many have proposed that they would be especially beneficial for type 2 diabetics trying to stabilize their blood glucose levels.[48,49,50] However, the long-term safety and efficacy of these diets remain largely unknown. Both the American Heart Association and the American Diabetes Association have cautioned against the use of these diets, pointing out that excess consumption of proteins and fats may promote hyperlipidemia, impaired insulin metabolism, and renal/liver malfunction.[26,27,28]

Unfortunately, little is known about the long-term effects of a low-carbohydrate diet on health. This study seeks to examine the current evidence for recommending a diet low in carbohydrates for type 2 diabetics. What impact does a low carbohydrate diet have on intermediate outcomes of health, including glycemic control, HgbA1c, weight reduction, insulin sensitivity, triglycerides (TGs), and lipid levels? Given the rising public interest in low carbohydrate diets, it is important that we know how newly proposed diets will affect type 2 diabetic patients.[103-104]

Methods

Selection Criteria

Randomized controlled trials in the English language of patients with a clinical diagnosis of type 2 diabetes were eligible if one of the following interventions were included: low-carbohydrate, ketogenic, high protein, or high fat diets. All interventions had to have a maximum carbohydrate content of 45% of total energy, a level that was arbitrarily selected to include most "low carbohydrate" diets in the scientific literature. Additionally, one of the following outcomes had to be measured in the study: glycemia control, glycated hemoglobin, insulin sensitivity, weight change, lipids, or triglycerides.

Studies were excluded if:

- Participants were not type 2 diabetics, unless stratified randomization and analysis was done separating the type 2 diabetic group from the non-type 2 diabetics.
- Participants were pregnant
- At least one outcome of interest was not incorporated.
- Diets were not sustained for at least 4 days duration
- Multiple diets were included in the same study

Search Strategy and Data Sources

Searches were performed on PUBMED for studies that were published between January 1, 1966, and March 16, 2004 and met the eligibility requirements. Studies indexed with the keywords such as *diet, diabetes,* and *low carbohydrate* were sought (see Table 1). I also reviewed bibliographies of retrieved articles to obtain additional citations.

Abstraction Methods

I reviewed 707 titles and abstracts identified by the combined MEDLINE search (see Table1). I extracted study design and participant data to identify those studies that met inclusion criteria. I excluded duplicate studies of the same participant group. I examined studies that included multiple diets or participant groups for separate analysis of the type 2 diabetics. I excluded the studies without separate analysis and study arms with diets not meeting inclusion criteria.

Data Abstraction

The author extracted three main types of data: 1) The dietary intervention, including percentage composition of carbohydrate, fat, and protein; 2) daily caloric content; and, 3) diet duration. Study data included total number of subjects, mean ages, and sex. The main outcome variables included weight change, glycemic control, glycated hemoglobin, insulin levels, and measures of serum lipid levels (low-density lipoprotein {LDL} cholesterol, high-density lipoprotein {HDL} cholesterol, and serum triglycerides.

Internal Validity Check

To assign grades to any recommendation, determine the strength of conclusions, or guide recommendations for future research, it is necessary to perform a quality assessment. The author performed a quality assessment starting at the point of study selection.

I contructed a modified version of Verhage's delphi list, a criteria list for the quality assessment of randomized clinical trials for conducting systematic reviews.[25] The first row of Table 2 delineates the aspects of this tool. The

included components capture generic methodological issues not just specific to the subject area being reviewed. Specifically, the assessment components determined if the studies:

- evaluated the similarity of baseline characteristics of the groups
- used effective means of randomization
- employed allocation concealment
- provided evidence of masking patients
- provided evidence of masking care providers
- provided evidence of masking outcome assessors
- provided point estimates of outcome variables with a measure of variability
- looked for protection against bias
- employed intention to treat analysis

I assigned an overall quality grade to each study; either poor, fair, or good. Good quality studies scored an "adequate" on at least four of the nine components, and included an adequate method of randomization and analyzed data on an intent-to-treat basis. Adequate approaches to randomization included central randomization, computer-generated random numbers or random number tables. Inadequate approaches included use of alternation, case record numbers, birth dates, or week days. A grade of unknown was reported for studies that simply included the word "randomized" without further detail.

I gave an overall quality grade of fair to those studies that received an adequate score on less than four components, or received an "unknown" on either

the approach to randomization or intent-to-treat analysis. A grade of poor was reserved for studies that had major design flaws, including an inadequate approach to randomization or data anlysis not performed on an intent-to-treat basis.

TABLE 1 Literature Search Strategy	
Description	Articles
MELINE key word searches	
Search 1, *diet**	282,781
Search 2, *diabetic*	103,706
Search 3, *NIDDM*	30,829
Search 4, *diabetes*	212,085
Search 5, *low carbohydrate**	645
Search 6, *high fat**	6,531
Search 7, *high protein**	3,807
Search 8, *ketogenic*	853
Search 9, *isocaloric*	2,951
Search 10, *hypocaloric*	753
Search 11, *protein sparing*	2,241
Search 12, *carbohydrate restricted*	6,908
Combine searches: 1 AND (2 OR 3 OR 4) AND (5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12) LIMIT to participant type: human	707
Exclusion Criteria	
Not an adult study	287
Articles not in English	73
Review articles	154
No dietary intervention	85
Study did not examine type 2 diabetes	76
Diet duration less than 4 days	47
No outcome of interest	95
Non-human trial	1
Inpatient study	5
Pregnancy study	10
Total articles excluded from those found in MEDLINE search	635
Articles included from manual search of bibliographies	2
Articles not available free of charge from UNC libraries	52
Total articles included in analysis	12
Combined duplicate reports on the same study participants	0

Table 2. Quality Assessment of Articles

Study	Randomization	Treatment allocation concealed?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors blinded?	Care provider blinded?	Patient blinded?	Point estimates and measure of variability presented for the primary outcome measure?	Intent to treat analysis?	Overall Quality
Ash et al.	Adeq	Unk	Reported	Adeq	Unk	Unk	Unk	Adeq	Adeq	Good
Facchini et al.	Adeq	Adeq	Reported	Adeq	Unk	Unk	Unk	Adeq	Adeq	Good
Gutierrez et al.	Adeq	Adeq	Reported	Adeq	Unk	Unk	Unk	Adeq	Adeq	Good
Hollander et al.	Unk	Unk	Reported	Adeq	Unk	Unk	No	Adeq	Adeq	Fair
Heilbronn et al.	Unk	Unk	Reported	Adeq	Unk	Unk	No	Adeq	Inad	Poor
Luscombe et al.	Unk	Unk	Reported	Adeq	Unk	Unk	Unk	Adeq`	Inad	Poor
Madigan et al.	Unk	Unk	Reported	Adeq	Unk	Unk	Unk	Adeq	Adeq	Fair
Markovic et al.	Unk	Unk	Reported	Adeq	Unk	Unk	Unk	Adeq`	Inad	Poor
Ozata et al.	Unk	Adeq	Reported	Adeq	Unk	Unk	Adeq	Adeq	Inad	Poor
Nuttall et al.	Adeq	Adeq	Reported	Adeq	Unk	Unk	No	Adeq	Adeq	Good
Parker et al.	Unk	Unk	Reported	Adeq	Unk	Unk	Unk	Adeq	Adeq	Fair
Samaha et al.	Adeq	Unk	Reported	Adeq	Unk	Unk	Unk	Adeq	Adeq	Good

Legend: Unknown=Unk; Adequate=Adeq; Inadequate=Inad

Table 3. Study Characteristics

Study	N	Participants Age, SD	Duration of Diet	Sex % Male	No. Of Study Arms	Total Kilocalories per Day	Carbs, g	Fat, g	Protein, g
Ash et al.	51	Men up to 70 years of age 54 +/- 9	12 wks	100	3	1400-1700			
Facchini et al.	100 91	59 (10) 60 (12)	4 yrs	53 48	2	.8 g/kg I control			
Gutierrez et al.	28 crossover design	67 (6.2) 67 (6.2)	7.9 wks 12 wks	29	2				
Hollander et al.	159 162	54.7 (9.7) 55.4 (8.8)	52 wks 52 wks	53 49	2	500 500			
Heilbronn et al.	55 Crossover design	56.0 (9.4) 57.5 (9.6) 56.0 (9.4) 57.5 (9.6)	4 wks 4 wks 8 wks 8 wks	46 57 46 57	2	1500 1500 1500 1500	 213 218	 31 30	 83 78
Luscombe et al.	11 15	64.2 +/-3.3 62.2 +/-2.2 SEM	8 wks 8 wks	55 33	2	1600 1600			60 110
Madigan et al.		56.0 (2.5) 56.0 (2.5)							
Markovic et al.	9	47.6 +/- 4.8	2 wks	44	2	1100	132	8	122
Ozata et al.	20	41.6 (8)	3 mon	100	2	1200-1400			
Nuttall et al.	12 Crossover design		5 wks 5 wks	83 83	1		299 223		
Parker et al.	54 Crossover design	63.4 +/- 1.7 64.2 +/- 3.8 63.4 +/- 1.7 64.2 +/- 3.8	8 wks 8 wks 4 wks 4 wks	35 36 35 36	2	1587 1543 2029 1785	36		
Samaha et al.	52	54 (9) 54 (10)	6 mon 6 mon	80 85	2	1630 1576	<30		<30%tot

Table 4. Outcomes of Interest

Study	Mean Reduction in intake	Diet C:F:P (% energy)	Duration of diet	Mean Age	Insulin Sensitivity as % change in insulin levels	Weight loss in kg	Glycemia Fasting blood change (mg/dl)	HgbA1c reduction	LDL change Mmol/l	TG change	HDL change
Ash et al.	564 +/- 665 kcal/day	50:30:20	12 wks	Men up to 70 years of age 54 +/- 9		6.4 +/- 4.6 SD		1.0 +/- 1.4%		TG - 0.3 +/- 0/6 mmol/l	
Facchini et al.		35:30:30:5 vs 65:25:10	4 years 4 years	59 (10) 60 (12)		2.0 1.0		N.S.	+. 007 -.012		+. 23 -.05
Gutierrez et al.		25:45:30 Vs. 55:20:25	7.9 wks 12 wks	67 (6.2) 67 (6.2)		1.4 (15) +1.0	-66 -74	1.8 1.0			
Hollander et al.	Orlistat	50:30:20 50:30:20	52 wks 52 wks	54.7 (9.7) 55.4 (8.8)	-4.3 +/- 6.3% -5.2 +/- 4.4%	4.3 +/-.5 6.2 +/-.5 SEM 95CI	-10 +/- 2 -15 +/- 2 SEM	.88 .83	+. 22 +/. 06 -.13+/-.05	.21+/-.08 -.01+/-.07	+. 08+/- .01 +. 06+/- .01
Heilbronn et al.	GI Index	50:30:20 50:30:20 60:15:20 60:15:20	4 wks 4 wks 8 wks 8 wks	56.0 (9.4) 57.5 (9.6) 56.0 (9.4) 57.5 (9.6)		3.3 4.0 4.4 4.8	4 9 6 4	.09 .31 .61 .29	-.07 -.12 -.54 -.34	-.45 -.13 -.12 -.18	+.01 +0 +. 01 +. 02
Luscombe et al.		55:30:15 40:30:30	8 wks 8 wks	64.2 +/-3.3 62.2 +/-2.2 SEM		4.3 +/-.7 4.9 +/-.4					
Madigan et al.		Not available	2 wks 2 wks	56.0 (2.5) 56.0 (2.5)							
Markovic et al.	1200 kcal/day	38:29:33	4 wks	47.6 +/- 4.8		6.2 +/-.4			-.55	-.21	
Ozata et al.			3 mon	41.6 (8)		1.97	-37				
Nuttall et al. Gannon et al.		55:30:15 40:30:30	5 wks 5 wks					-.3 -.8			
Parker et al.	+442 kcal +242 kcal	40:30:30 60:25:15 40:30:30 60:25:15	8 wks 8 wks 4 wks 4 wks	63.4 +/- 1.7 64.2 +/- 3.8 63.4 +/- 1.7 64.2 +/- 3.8	-26% -15% -11% +6%	4.5 4.5 1.1 .3	-18 -12 6 5	-.54 -.51	-.30 -.12 +. 11 +. 20	-.48 -.41 +. 12 +. 18	-.01 -.04 0 +. 05
Samaha et al.	460 271	37:41:22 51:33:16	6 mon 6 mon	54 (9) 54 (10)	-20 (75) 0 (56)		-26 (31) -5 (31)	-.6 (1.2) 0 (1.0)			

III. Results

Articles Identified

My MEDLINE search identified a total of 707 potentially eligible articles. Reference searching identified two additional studies. After abstract review, a total of 64 articles met the inclusion criteria. Twelve of these articles were available free of charge through UNC libraries and were included in the analysis (Table 1).

Quality of the Studies

The modfied version of the Delphi list, a criteria list for the quality assessment of randomized clinical trials for conducting systematic reviews was applied to the identified studies. Table 2 summarizes the results of this assessment. Overall, five of the 12 studies received a grade of good. Three of 12 received a grade of fair, and the remaining four had a major methodological flaw and received a grade of poor.

All 12 of the identified studies clearly specified the eligibility criteria. All 12 reported similar baseline characteristics of the groups initially and presented point estimates and a measure of variability for the outcomes of interest. Only four of the studies clearly stated the method of randomization; the other eight simply employed the word "randomized." The treatment allocation was determined to be blinded from the physicians in only four of the studies; the other eight did not provide enough information to deduce this. None of the studies stated whether the outcome assessors were blinded.

Four of the 12 did not employ intent-to-treat analysis, and received the grade of "poor" overall quality. The four "poor" quality studies are excluded from subsequent analysis and discussion in this review.

Study Characteristics

The eight "fair" or "good" quality studies included a total of 18 different dietary interventions (Table 3). All of the studies were randomized controlled trials in which the patients were randomized to one of two or more dietary interventions. Additionally, the studies varied in design, as three of the studies were crossover designs. In these three studies, the patients first were randomized to receive one diet, then after a specified period of time received a second diet. The number of participants in the studies ranged from 12 to 391.

Some of the diets included a washout phase at the beginning of the study during which patients received s standard diet intended to mimic their normal diets in caloric and carbohydrate content. In these studies, the weight at end of washout period was recorded as the patients' baseline weights.

Diet Characteristics

The dietary interventions were also highly heterogeneous. The duration of the diets ranged from 4 weeks to 52 weeks (Table 4). Furthermore, the average number of kilocalories per day ranged from 500 kcal/day to 2029 kcal/day (Table 3). The percentage of carbohydrate in the diets ranged from 25% to 65% of total energy, and only five of the eight "fair" or "good" quality diets included the total daily kilocalorie intake. Five of the diets reported dietary composition ranges in grams of carbohydrates, proteins, and fat.

Most of the dietary interventions prescribed a diet and had the patients keep a daily log. This self-reported log was used to calculate the actual dietary interventions' total calories and amount of carbohydrate in diet. A few studies actually provided prepackaged meals to ensure that participants received precisely the prescribed dietary intervention. The Madigan dietary intervention included a significant amount of linoleic acid-rich sunflower oil in the diet.

Patient Characteristics

The average age of participants in the different studies ranged from 41.6 to 67 years (Table 3). Two of the studies examined only men. The Facchini study recruited a cohort of more advanced type 2 diabetic patients referred to nephrology clinics for various degrees of renal failure and otherwise unexplained proteinuria. The Gutierrez study included an arm of patients treated with second-generation sulfonylurea agents. The Parker study excluded patients with any degree of proteinuria.

Several of the studies were limited to patients with varying degrees of obesity. For example, the Ash cohort included men with a body mass index (BMI) between 25 and 40. The Hollander study included patients with a BMI ranging between 28 and 40, and the Samaha study cohort included only severely obese patients with an average BMI of 43.

Outcome Measures for the Low-Carbohydrate Interventions

Three of the studies reported insulin sensitivity as a percent change in serum insulin levels. The Parker study showed a greater decrease in serum insulin levels in the two arms that had lower carbohydrate contents (60% versus 40%). The Samaha study, which included an arm with 37% carbohydrate content, showed a decrease in serum insulin level compared to the 51% carbohydrate arm, which showed no change. The Hollander study included two 50% carbohydrate arms which both showed a comparable decrease in serum insulin levels

Change in weight was reported in all but two of the studies. Most of the studies showed weight loss of varying degrees. The weight in most of the studies was usually greater in the low carbohydrate groups.

Fasting blood glucose levels also dropped in most of the studies. In the Guitierrez, Parker, and Samaha studies, the decrease in fasting blood glucose was greater in the lower carbohydrate containing diets.

All of the diets demonstrated a reduction in glycated hemoglobin A1c levels, except for the Facchini study, which failed to demonstrate any significant increase or decrease. The Gutierrez, Nuttall, Samaha, and Parker studies showed a greater reduction in the low carbohydrate arm

The lipid findings were equivocal. The Facchini study found a greater drop in LDL in the high carbohydrate containing arms, but Parker found the converse. The Parker study demonstrated an increase in LDL levels in two of the arms, which was greater in the higher carbohydrate-containing arm. Similar equivocal results were found for triglyceride levels

A change in HDL levels was reported in three of the dietary interventions. Facchini show an increase in the 35% carbohydrate-containing arm, but a decrease in levels in the 65% carbohydrate-containing arm. Parker showed a small increase in one 60% carbohydrate-containing arm, compared to no change in the 40% containing arm. The other two Parker arms both showed decreases in HDL levels, with a greater decrease in the 60% containing arm.

IV. Discussion

Based on the current studies, the evidence suggests that adherence to a low carbohydrate diet of at least four days duration may lead to weight loss and lower serum insulin levels. However, the data are equivocal for the other intermediate outcomes, including serum glucose levels, hemoglobin A1c, and lipid levels.

There is variability among studies with regard to internal validity. Many studies may be biased due to unsuitable comparison interventions, lack of blind outcome assessment, inadequate follow-up times, and inability to define or assess relevant outcomes, or unreliable measurement techniques. The variation in the quality of selected primary studies has implications for data synthesis, interpretation of results, and generation of inferences in this review.

For example, the Gutierrez study's crossover design makes interpretation of results difficult. Patients are first on low carbohydrate/high fat diet, and then cross over to a higher carbohydrate containing diet. Measuring the change in outcome variables using data from the beginning of the low carbohydrate diet period may not be valid, as patients were not eating their normal diet at that time. This problem was not unique to the Gutierrez study, as some of the other studies had run-in periods while others did not. Prescribing a particular dietary intervention to a patient at the clinic cannot be based upon changes from a run-in period diet, unless that diet reflects what the patients normally consume. In this way, run-in periods and crossover designs may hurt the external validity of the studies' results.

Many of the studies were small and had limited power to detect significant differences in between intervention groups. In fact, few of the differences in outcomes outside of weight loss were significant. Over half the studies had less than 60 total participants. Difficulties and complexities in monitoring the dietary intake of individuals are likely to be one reason the studies have been small to date. A meta-analysis would be useful but extremely difficult to conduct due to the heterogeneity of the individual interventions.

The Ash study and Samaha study both suffered drop-outs. The Ash study lost only 5 of 51 patients to follow-up. The subjects lost were similar between groups and were comparable to the original population with regards to baseline characteristics. The Samaha study had a much higher drop-out rate, losing 53 of 132 patients to follow-up, and used last observation carried forward for those who dropped out. Although the study showed an increase in insulin sensitivity and improved glycemic control markers, it is possible the results were influenced by the high drop-out rate. Thirty-two of the 53 drop-outs came from the higher carbohydrate group. It is possible that individuals compliant with the higher carbohydrate (and lower fat-containing) diet were more likely to drop-out from the study than

individuals who were less compliant. This could skew results if those compliant individuals would have lost weight and reaped some of the clinical benefits associated with weight loss.

Additionally, many of the studies provided prepackaged meals to participants, which means larger trials would cost significantly more. Furthermore, supplying participants with prepackaged meals is a threat to the study's external validity. A physician or dietician in the field prescribing a low carbohydrate diet to a patient will likely not be supplying the prepackaged meals to ensure compliance, and application to long-term therapy is limited by the patients' willingness to pay for prescribed meals. Regardless, the use of prepackaged meals for a short period of time was thought to transfer knowledge of appropriate portion sizes and food types to patients. However, the Ash study included a subsequent follow-up 15 months after the free supply of prepackaged meals to patients was discontinued, and the weight loss was not sustained in the long term. This result is consistent with previous studies providing prepackaged meals.[51]

Another factor that contributes to the heterogeneity and makes comparisons more difficult among studies is the fact that some of the studies use the simple prescription of a particular diet as the intervention, while others relied on a dietary recall or diary to evaluate whether the patients actually followed the prescribed diet. Still others provide prepackaged meals to avoid recall bias and ensure the accuracy of data. It is likely that patient adherence varies between the different dietary intervention types. The studies relying solely on the prescription of a diet may have the most external validity, as that is what physicians and dieticians will be doing in the field.

However, it is important that we not draw conclusions about the efficacy of a low carbohydrate diet from studies relying on dietary recall to ensure compliance. Sources of error in short-term dietary recalls and records have been well documented.[40, 41] Most the studies included in this review relied on

subject recall or records, and are thus subject to several biases.[40] These errors may be respondent or recorder based.

Respondent based errors stem from the fact that accurate recall depends on several factors. The respondents must be motivated, aware of their food intake, and have adequate memory and communication skills. One study found that respondent knowledge of the study's purpose affected the measurement of food intake.[41] The same study also showed that respondent fatigue, related to length of survey, influenced results. Another study showed that continual contact with physicians increased the accuracy of the reports.[42] A third study found that men frequently did not list all the food they consumed because they were embarrassed to admit how much they had consumed.[43] All of these respondent based errors affect the external validity of the studies.

Many of the studies in this review relied on dietary logs with the subject using household measures to estimate the quantity eaten (i.e. a "fistful" of beans, or even more inaccurate, a "large or small" portion). These household measures are then converted to grams by the investigators. However, the type of conversion inevitably leads to a loss of precision. A study by Guthrie et al. found that amounts of butter, salad dressing, cereal, and salads were overestimated by more than 51% over two-thirds of the time, and the intake of salad dressings, butter, sugar, and salad were underestimated by at least 51% a quarter of the time.[44] To make matters worse, some specific types of foods tend to be erroneously recalled while others tend to be erroneously omitted. A 1985 study found that cooked vegetables tend to be omitted more frequently than other types of food, while sugar containing foods tend to be erroneously recalled more frequently.[45]

A study by Prentice et al. compared the energy expenditures of a group of lean and a group of obese women with their self-reported dietary records.[46] They used isotopically measured total energy expenditures and found that the obese group had a 28 percent higher daily energy expenditure than the

lean group, but tended to underestimate their intake by 837 kcal/day. The lean group accurately self-estimated their intake. This bias has significant implications for this review, as many of the included studies were of obese patients. If obese patients tend to underreport the amount of carbohydrate they consume and low-carbohydrate diets contribute to a feeling of satiety, then it is possible that control groups eating higher amounts of carbohydrate are underreporting their consumption in some of the studies.

Frank et al. found that the amount of training an interviewer receives can effect the amount of food recalled, and thus has implications for comparing the results of more than one study.[47] Well-trained interviewers using a detailed protocol substantially improved the reliability and reproducibility of dietary recalls. Furthermore, the behavior of the interviewer may affect results, especially if more than one interviewer is used in a study.[40] The manner of asking questions can affect answers, and the resulting information may vary depending on whether the probing is general or detailed. This facet undoubtedly contributes to the heterogeneity of the studies. Unfortunately, very few of the studies state what kind of training the interviewers received in detail, or how many different interviewers were used.

Studies of prescribed diets, which measure effectiveness, may provide more externally valid results, as this is what health care professionals will be doing in the field. Furthermore, dietary prescriptions that require patients to keep a log of their meals may not be comparable to prescription alone, as there may be benefit in requiring subjects to write down their intake daily. All of these factors make comparisons and conclusions a very messy business.

Most of the studies are consistent with the hypothesis that weight loss produces improvements in glycemic control. In general, the most hypocaloric diets seem to have better results. However, the included diets in this review were not isocaloric. Additionally, the low-carbohydrate diets vary significantly with calorie intake from carbohydrates. This heterogeneity makes it difficult to compare

diets. Since only one of the diets reported the main reduction in caloric intake from baseline (Ash et al.), it is difficult to ascertain whether the beneficial effects in any of the outcome variables are due to the implementation of a low carbohydrate diet or a low caloric diet which leads to weight loss in general.

Conversely, some authors hypothesize that dietary interventions that are low in carbohydrate lead to weight loss because more fat or protein helps provide a feeling of satiety. Patients on low carbohydrate diets may consume less food and less overall total calories compared to a higher carbohydrate diet. Less overall caloric intake then leads to weight loss, and we see the usual benefits associated with weight loss. If this is true, then setting up randomized controlled trials with isocaloric diets would negate the satiety effects of the diet and intervention group would be similar to the control group.

Source of error

If I were to publish this systematic review, a huge potential bias exists. After abstract review, a total of 68 articles were identified that may have met the inclusion criteria. Fifty-two of these were not available free of charge. Of the 16 that were acquired, only 12 of these (75%) met the inclusion criteria after careful examination. Thus, of the remaining 52 unacquired articles, if 75% of these truly met the inclusion criteria, 36 articles were omitted. It is noteworthy that the UNC health science library provides free access to the more reputable journals, and it is likely the included studies are of higher quality than the omitted studies.

Conclusion and Recommendation

In conclusion, the data regarding the effectiveness of low carbohydrate diets for type 2 diabetics are limited. The studies have been small, of varying quality, and very heterogeneous with respect to dietary interventions and methodology. Weight loss, in general, is probably beneficial for type 2 diabetics. However, there is insufficient evidence to recommend for or against the specific use of low

carbohydrate dietary interventions in type 2 diabetics. Larger studies of better quality must be conducted and methodology must be standardized to allow pooling of data. It is possible that the dietary interventions must stay below a maximum threshold of dietary carbohydrate for benefits to be elicited. Furthermore, new variables such as the glycemic index of the carbohydrates included in the diet or what food replaces the carbohydrates may be equally important. Future research must address these questions.

Based on the current evidence, it is this author's opinion that type 2 diabetics should be counseled that weight loss in general will be beneficial, providing them with numerous well documented health benefits. If individuals wish to pursue weight loss through a low carbohydrate diet, physcians should advise them that conslusive evidence of their benefits independent of weight loss is lacking, and that the long term effects of low carbohydrate diets are largely unknown.

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